

### REMARKS

The Applicants thank the Examiner for his careful analysis of the instant application. Claims 1-27 and 30-43 stand rejected and claims 28 and 29 are objected to. The Applicants have amended the claims as shown above and submit that in light of the forgoing amendments and following comments, the application is now in proper form for allowance.

The Examiner has rejected claims 1, 7, 16, 26 and 41 under 35 U.S.C. §112, ¶2 as being indefinite for failing to point out and distinctly claim the subject matter. The Applicants have amended claims 1, 16, 26 and 41 as set forth above to delete the phrase "such as blood and plasma," making the claims definite. Claim 7 has been amended to state that the device "comprises a biological fluid loop" providing proper antecedent basis for "the biological fluid loop" later in the claim. The Applicants submit that the amendments do not alter the scope of the claims as they have been made only to increase clarity. The Applicants submit that the amended claims now distinctly point out the subject matter to be claimed, thus the rejection under 35 U.S.C. §112, ¶2 is traversed.

The Examiner has rejected claims 1-2, 7-8, 12, 14-17, 21, 24-27, 32, 35, 37-38 and 41-42 under 35 U.S.C. §102(b) for being anticipated by Olumide et al. Olumide et al teach an artificial liver apparatus comprising many of the same elements as the instant invention. The Examiner has further rejected claims 18-20 for obviousness under 35 U.S.C. §103(a) in view of the same reference.

The Examiner has rejected claims 3-6, 9, 11, 22-23, 30-31, 33 and 43 under 35 U.S.C. §103(a) as being unpatentable over Olumide in further view of US Patent 5,043,260. Claims 10 and 34 are rejected under 35 U.S.C. §103(a) as being unpatentable over Olumide in further view of US Patent 4,335,994. Claims 13 and 36 are rejected under 35 U.S.C. §103(a) as being unpatentable over Olumide in

further view of US Patent 5,001,607. Claims 39-40 are rejected under 35 U.S.C. §103(a) as being unpatentable over Olumide in further view of Arnaout et al.

The Examiner stated that claims 28-29 are objected to for being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim. The Applicants have amended all of the independent claims in the case, claims 1, 16, 26 and 41 to contain the limitation of claim 28. Therefore the new independent claims should all be allowable. Claim 29 has been amended to depend on the now allowable claim 26. As all of the remaining claims are dependent on the now allowable claims, all of the rejections under 35 U.S.C. §102(b) and 35 U.S.C. §103(a) are traversed.

#### **FEES**

The Applicants have enclosed a check for \$483 for a three month extension for the filing of a response (\$465) and two new dependent claims (\$18, 3 new - 1 cancelled = 2). It is believed that no additional fee is due with this response. However, if a fee is due, the Commissioner is hereby entitle to charge Deposit Account 02-4070 referencing case number 7728-PA01.

#### **CONCLUSIONS**

The Applicants submit that in light of the forgoing amendments and comments that all of the objections and rejections have been overcome or traversed

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and that the application is now in the proper form for allowance. If any outstanding issues remain that could be resolved by a telephone conference, the Examiner is encouraged to telephone the Agent for Applicant at the number below.

Respectfully submitted,

Dated: April 1, 2003

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Docket No.: 7728-PA01

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

1. (Amended) A device for extracorporeal purification of mammalian biological fluid [such as blood and plasma] comprising;

a bioreactor having inlet and outlet ports for, respectively, ingress and egress of biological fluid; inlet and outlet ports for, respectively, ingress and egress of culture medium; and at least one semipermeable membrane extending therethrough, which membrane defines a first conduit for ingress and egress of biological fluid and a second conduit for ingress and egress of culture medium;

a mixing vessel in fluid communication with the second conduit, wherein the mixing vessel has an inlet port for introduction of living, unattached hepatocytes into the culture medium;

a metal containing substrate for attachment of hepatocytes;

oxygenation means in gaseous communication with the mixing vessel;

pump means for circulation of biological fluid through the first conduit of the bioreactor; and,

pump means for circulation of hepatocytes and culture medium in the mixing vessel and through the second conduit of the bioreactor.

7. (Amended) The device according to Claim 1 further comprising a biological fluid loop, wherein the biological fluid loop is composed of material compatible with fluids selected from the group consisting of blood, plasma and plasma containing plasma extenders.

16. (Amended) A method for extracorporeal purification of a biological fluid [such as blood and plasma], the method comprising:

introduction of at least a theoretical minimum number of living, unattached

hepatocytes into a mixing vessel, wherein the mixing vessel is filled with culture medium and is free of air;

incubation to allow attachment of hepatocytes to a metal containing substrate;

circulation of the biological fluid through the bioreactor; and,

circulation of the hepatocytes and culture medium in and from the mixing vessel through a bioreactor having at least one semipermeable membrane passing therethrough, wherein the membrane separates the culture medium from the biological fluid but allows solutes to pass from the biological fluid into the culture medium.

26. (Amended) A device for extracorporeal purification of mammalian biological fluids [such as blood and plasma] comprising:

a bioreactor having and inlet and outlet ports for, respectively, ingress and egress of biological fluid; inlet and outlet ports for, respectively, ingress and egress of culture medium; and at least one semipermeable membrane extending therethrough, which membrane defines a first conduit for ingress and egress of biological fluid and a second conduit for ingress and egress of culture medium;

a port in fluid communication with the second conduit for introduction of living hepatocytes attached to a substrate into the culture medium;

pump means for circulation of biological fluid through the first conduit of the bioreactor; and,

pump means for circulation of hepatocytes and culture medium into and through the second conduit of the bioreactor wherein at least a portion of the hepatocytes are attached to a metal containing substrate.

29. (Amended) The device according to claim 26 [28] further comprising means for generating an alternating magnetic field wherein the field will cause the metal containing substrate to be circulated within the bioreactor.

41. (Amended) A method for extracorporeal purification of a biological fluid [such as blood and plasma], the method comprising:

introduction of at least a theoretical minimum number of living hepatocytes into a first conduit of a bioreactor;

incubation to allow attachment of hepatocytes to a metal containing substrate;

circulation of the biological fluid through a second conduit of the bioreactor, wherein the first and second conduits are separated by a semi-permeable membrane; and,

circulation of the hepatocytes in the first conduit of the bioreactor.

44. (New) The device according to claim 1 further comprising means for generating an alternating magnetic field wherein the field will cause the metal containing substrate to be circulated within the bioreactor.

45. (New) The method according to claim 16 further comprising application of an alternating magnetic field to cause the metal containing substrate to be circulated within the bioreactor.

46. (New) The method according to claim 41 further comprising application of an alternating magnetic field to cause the metal containing substrate to be circulated within the bioreactor.